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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,677	05/31/2002	Joerg Schneider	3022.1004-000	4825

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EXAMINER	
ZEMAN, ROBERT A	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
09/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/088,677	SCHNEIDER ET AL.	
	Examiner	Art Unit	
	ROBERT A. ZEMAN	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 June 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-21* is/are pending in the application.

4a) Of the above claim(s) *9 and 14-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10-13 and 17-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6-9-2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The response filed on 6-9-2008 is acknowledged. Claims 9-21 are pending. Claims 9 and 14-16 remain withdrawn from consideration as being drawn to non-elected inventions. Claims 10-13 and 17-21 are currently under examination.

Information Disclosure Statement

The Information Disclosure Statement filed on 6-9-2008 has been considered. An initialed copy is attached hereto.

Claim Rejections Maintained

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

The provisional rejection of claims 10-11 and 18 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 10/686,943 is maintained for reasons of record.

As outlined previously, although the conflicting claims are not identical, they are not patentably distinct from each other because both claim sets are drawn to methods of generating a CD8+ T cell immune response utilizing priming and boosting compositions comprising viral vectors wherein said vectors contain DNA encoding T cell epitopes of a given antigen. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

It should be noted that Applicant has indicated that they will not address this rejection until an indication of allowable subject matter has been made.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 10-13 and 17-21 under 35 U.S.C. 103(a) as being unpatentable over McMichael et al. (WO 98/56919) and Kazanji et al. (International Journal of Cancer, 1997, Vol. 71, pages 300-307 -- IDS filed on 3-21-2002) is maintained for reasons of record.

Applicant argues:

1. The rejection is based on the incorrect interpretation of certain sentences in the Kazanji et al. reference.

2. A close reading of the Kazanji et al. references reveals that Kazanji et al. did not perform a heterologous prime-boost regiment using a DNA plasmid prime and an adenovirus vector boost, nor do they suggest such a regimen.

3. If Kazanji et al. had performed the aforementioned prime-boost regimen it is expected that it would be indicated in Table I (A, B or C) or in one of the other figures.

4. McMichael disclose methods of generating a CD8+ T cell response against a target antigen utilizing a priming composition comprising a source of one or more CD8+ T cell epitopes of an antigen and a boosting composition comprising one or more CD8+ T cell epitopes encoded by a non-replicating or replication-impaired recombinant poxvirus vector and not the instant adenovirus vectors of the instant invention.

5. The combined teachings of the references would not motivate one of skill in the art to substitute the poxvirus vector of McMichael with the adenovirus vector of Kazanji et al. since Kazanji et al. teach away from using an adenovirus vector in a heterologous prime-boost method.

6. There is no teaching or suggestion in McMichael et al. or Kazanji et al. to suggest the desirability of using the adenovirus vector of Kazanji et al. in the heterologous prime-boost method of McMichael et al.

Applicant's arguments have been fully considered and deemed non-persuasive.

In response to Points 1-3, contrary to Applicant's assertion, Kazanji et al. explicitly disclose that WKY rats were primed with DNA plasmids containing the HTLV-1-*env gp46* gene and boosted with Ad5 containing the HTLV-1-*env gp46* gene (see abstract, bridging paragraph of columns 1 and 2 on page 303 and column 2 of page 304). Moreover, Kazanji et al. also disclose that rats that had previously been primed with DNA plasmids containing the HTLV-1-*env gp46* gene or with Ad5 containing the HTLV-1-*env gp46* gene where further boosted with either HTLV-1-*env gp46* gene or Ad5 containing the HTLV-1-*env gp46* (see page 303, first paragraph). Consequently, Kazanji et al. disclose the efficacy of adenovirus vectors as boosting compositions. Finally, Applicant is reminded that not all methods/results are presented within Tables.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

In response to applicant's argument that there is no suggestion to combine the references (Points 5 and 6), the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some

teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, one would have been motivated to use the adenovirus vectors disclosed by Kazanji et al. in the compositions and methods disclosed by McMichael et al. in order to take advantage of the ability of the adenovirus vectors to be orally administered and to be cheaply made. One would have had a reasonable expectation of success since Kazanji et al. disclose that WKY rats primed with pMLP-KTLV-I-*env* and posted with Ad5-HTLV-I-*gp46* induced a CTL response against HTLV-I transformed cells (see page 304, column 2).

As outlined previously, McMichael et al. disclose methods of inducing a CD8 T cell immune response comprising the administration of a priming composition and a boosting composition wherein said boosting composition comprises a non-replicating or replication impaired pox virus vector (see abstract). Moreover, McMichael et al. further disclose the priming composition can comprise a nucleic acid (either DNA or RNA) that is packaged or in free form (see page 11, lines 4-8), Ty-VLP or a recombinant adenovirus (see page 12, lines 4-5). McMichael et al. further disclose that the MVA can be used (see page 12, lines 6-9) in both the priming and boosting compositions (see page 13, line 29-30) and that a variety of viral vectors (including herpes virus) can be used in the priming composition (see page 13, lines 7-16).

McMichael et al. differs from the instant invention in that they do not explicitly disclose the use of boosting compositions comprising non-replicating or replication impaired adenovirus vectors.

Kazanji et al. disclose the administration of naked DNA plasmids containing the HTLV-I-*env* gene as the "primer" and the administration of Ad5 containing the HTLV-I-*env gp46* gene as the "booster" (see abstract). Moreover, Kazanji et al. disclose that adenovirus vectors have the potential for oral immunization, are cheaply produced and have been successfully used in vaccines against EBV (see page 300. left hand column).

Consequently it would have been obvious for one of ordinary skill in the art at the time the invention was made to use the adenovirus vectors disclosed by Kazanji et al. in the compositions and methods disclosed by McMichael et al. in order to take advantage of the ability of the adenovirus vectors to be orally administered and to be cheaply made.

One would have had a reasonable expectation of success as adenovirus vectors have been successfully used in other vaccine compositions and in prime-boost methodologies (see Kazanji et al. since Kazanji et al. disclose that WKY rats primed with pMLP-KTLV-I-*env* and posted with Ad5-HTLV-I-*gp46* induced a CTL response against HTLV-I transformed cells (see page 304, column 2).

The rejection of claims 10-13 and 17-21 under 35 U.S.C. 103(a) as being unpatentable over McMichael et al. (WO 98/56919) and Natuk et al., 1993, AIDS Research and Human Retroviruses, Vol. 9 No. 5, pages 395-404 -- IDS filed on 3-21-2002) is maintained for reasons of record.

Applicant argues:

1. The combined teaching of the cited references do not suggest that substituting the non-replicating or replication impaired recombinant poxvirus vector in the method of McMichael et

al. would yield a predictable or successful induction of a CD8+ T Cell immune response to antigen.

2. Natuk et al. do not teach that the induction of antibodies to adenovirus is a drawback of using replication competent adenovirus.

3. The success of Ad7-HIV attest to the potential safety of the replication-competent Ad7 vector and do not teach or suggest that neutralizing antibodies are induced by immunization with replicating adenovirus.

4. McMichael et al. disclose that the efficacy of non-replicating or replication impaired poxvirus vectors was surprising and could not be predicted based on the teachings of the prior art.

5. McMichael et al. do not disclose that said "unexpected results" could be achieved using any non-replicating or replication-impaired viral vector other than the disclosed pox virus vector.

6. Natuk et al. does not teach or even suggest that the use of a replication-deficient adenoviral vectors would yield a predictable result.

Applicant's arguments have been fully considered and deemed non-persuasive.

In response to Points 1, 2 and 6, Natuk disclose not only the efficacy of replication deficient adenovirus vectors but also disclose the drawbacks of using replication competent adenoviruses (which would necessarily include the induction of circulating neutralizing antibodies.

With regard to Point 3, Natuk et al. specifically disclose there are drawbacks in utilizing replication-competent adenoviruses. Said drawbacks would be obviated by using non-replicating vectors as disclosed by McMichael et al. Taken with the disclosure of McMichael et al., the

skilled artisan would have been motivated to use replication-deficient adenoviruses in the methods of McMichael et al.

With regard to Point 4 and 5, in view of the KSR decision, since the use of replication-deficient adenovirus vectors is well known in the art yielding predictable results, it is obvious for the skilled artisan to use them in the methods of McMichael et al. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]).

As outlined previously, McMichael et al. disclose methods of inducing a CD8 T cell immune response comprising the administration of a priming composition and a boosting composition wherein said boosting composition comprises a non-replicating or replication impaired pox virus vector (see abstract). Moreover, McMichael et al. further disclose the priming composition can comprise a nucleic acid (either DNA or RNA) that is packaged or in free form (see page 11, lines 4-8), Ty-VLP or a recombinant adenovirus (see page 12, lines 4-5). McMichael et al. further disclose that the MVA can be used (see page 12, lines 6-9) in both the priming and boosting compositions (see page 13, line 29-30) and that a variety of viral vectors (including herpes virus) can be used in the priming composition (see page 13, lines 7-16).

McMichael et al. differs from the instant invention in that they do not explicitly disclose the use of boosting compositions comprising non-replicating or replication impaired adenovirus vectors.

Natuk et al. disclose the use of vaccines comprising recombinant adenoviral vectors in prime-boost protocols (see abstract). Natuk et al. further disclose that human adenoviruses possess significant advantages as vectors for recombinant vaccines including a strong safety

record and multiple serotypes that can be exploited as vectors for booster immunizations (see pages 395 right hand column to page 396 left hand column).

Consequently it would have been obvious for one of ordinary skill in the art at the time the invention was made to use the adenovirus vectors disclosed by Natuk et al. in the compositions and methods disclosed by McMichael et al. in order to take advantage of the safety and versatility associated with adenovirus vectors. Moreover, it would have equally obvious to render the adenovirus vectors replication-deficient in order to take advantage of their increased safety (as disclosed by McMichael et al.).

One would have had a reasonable expectation of success as adenovirus vectors have been successfully used in vaccines for the prevention of acute respiratory disease (see page 396 in Natuk et al.). Moreover, in view of the KSR decision, since the use of replication-deficient adenovirus vectors is well known in the art yielding predictable results, it is obvious for the skilled artisan to use them in the methods of McMichael et al. (see *KSR International Co. v. Teleflex Inc.*, No. 04-1350 [U.S. Apr. 30, 2007]).

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ROBERT A. ZEMAN whose telephone number is (571)272-0866. The examiner can normally be reached on Monday- Thursday, 7am -5:30 p.m. .

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Mondesi can be reached on (571) 272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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/Robert A. Zeman/
Primary Examiner, Art Unit 1645
September 25, 2008